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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,663	02/27/2002	A. K. Gunnar Aberg	559P017	3512

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,663	ABERG ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-10,13-15,18,19 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1,7-10,13-15,18,19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 6-10, 13-15, 18, 19, 21 are pending. Claims 4, 5, 16, 17 have been canceled according to the amendment filed on 7-25-2003. Claims 2, 3 have been cancelled according to the amendment filed on 3-22-2004. Claims 11, 12, 20 have been canceled according to the amendment filed on 1-10-2005.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-10-2005 has been entered.

Claim Rejections - 35 USC § 103

3. The 103(a) rejection over Polivka I (CS 263993) or Polivka II (Coll. Czech. Chem. Commun. 1989, 54(9), 2443-69, PTO-1449) in view of Le Bigot (Life Sciences, 40, 883-890, PTO-1449) and Bourquin (3862156, PTO-1449) and Kofler (Experimental Chemistry. Organic Chemistry and Reaction. Pages 504-505, PTO-1449) is withdrawn in view of Applicant's remarks and the amendment incorporating the limitation of the S-isomer of a metabolite of ketotifen being substantially free of the corresponding R isomer.

Claim Rejections - 35 USC § 112(1)

4. The rejection under 35 U.S.C. 112, first paragraph is maintained for reasons of record.

The amendment limiting the method to treatment of allergic disorders, inflammatory disorders of the skin, the respiratory tract and the gastrointestinal tract fails to overcome the rejection, as each of these is a class disorders encompassing diseases of diverse origins, including

the as yet unidentified allergic disorders, inflammatory disorders of the skin, the respiratory tract and the gastrointestinal tract. Furthermore, a description of inflammatory disorders of the skin, the respiratory tract and the gastrointestinal tract is not found in the specification (see paragraph 6 below). One of ordinary skill in the art would not be able to use the inventive compound to treat all these disorders without undue experimentation.

Claim Rejections - 35 USC § 102

5. The rejection under 35 U.S.C. 102(a) over Aberg I (WO 98/56381) or Aberg II (WO 98/43640, PTO-1449) is withdrawn in view of the amendment incorporating the limitation of S – norketotifen substantially free of the R isomer, thereby setting a demarcation from the prior art compositon.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-10, 13-15, 18, 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, the description for 'the pharmaceutical composition comprising the *S-isomer of a metabolite of ketotifen*, and having the structure.....and *being substantially free of the corresponding R-isomer*' is not found in the specification.

The description for 'inflammatory disorders of the skin, the respiratory tract and the gastrointestinal tract' in claim 7 is not found in the specification. The rejection is applicable to claims dependent on claim 7.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7-10, 13-15, 18, 19, 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1, 7, 21, the meaning of the term 'substantial' in 'substantially free of the corresponding R isomer' is unclear, as a definition of which is not found in the specification.

b. Claim 8, some of the recited disorders/conditions, such as cough, asthma etc., are usually not considered by one of ordinary skill in the art to be inflammatory disorders.

c. Claim 10, is not urticaria an allergic disorder according to claim 9 ?

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7-10, 13, 15, 18, 19, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aberg I (WO 98/56381) or Aberg II (WO 98/43640, PTO-1449) in view of Polivka I (CS 263993) or Polivka II (Coll. Czech. Chem. Commun. 1989, 54(9), 2443-69, PTO-1449).

Aberg I (page 2) or II (page 6) discloses norketotifen as an anti-inflammatory or anti-histaminic agent.

While Aberg I or II does not recite the S-norketotifen substantially free from the corresponding R isomer as in the instant, it is well known in the art that a compound can only be

in the form of the S, R or the racemic form and one optical isomer would have more desirable biological activity than the other or the racemic mixture. The separation of the R and S forms is routine for the skilled in the art. Ketotifen, the precursor of norketotifen, is known to be optically active, as pure enantiomers of ketotifen and their biological activities are described in Polivka I (pages 7-10, Examples 1, 3) and in Polivka II (page 2456-7). Accordingly, one of ordinary skill in the art would expect norketotifen to be optically active and the method for resolving the precursor ketotifen would be applicable for the separation of the S and R forms of norketotifen in view of their structural similarity.

At the time of the invention, one of ordinary skill in the art would be motivated to resolve the optical isomers of norketotifen and prepare the anti-inflammatory or anti-histaminic pharmaceutical composition comprising an optical isomer, such as the S-isomer to arrive at the instant invention. The absence of sedative side effect would inherently flow from its use as an antihistamine or an anti-inflammatory agent.

Double Patenting

9. The rejection for Claims 7, 9, 10, 12, 13-15, 18-20 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6207684 (the US equivalent to WO 98/56381) is withdrawn in view of the amendment deleting ocular disease from the instant claims, thereby setting a demarcation from the patented method.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of U.S. Patent No. 6207684 in view of Polivka I (CS 263993) or Polivka II (Coll. Czech. Chem. Commun. 1989, 54(9), 2443-69, PTO-1449).

The patented composition comprises an anti-inflammatory or antihistaminic norketotifen instead of the S-norketotifen substantially free from the corresponding R isomer as recited in the instant. However, it is well known in the art that a compound can only be in the form of the S, R or the racemic form and one optical isomer may have more desirable biological activity than the other or the racemic mixture. The separation of the R and S forms is routine for the skilled in the art. Ketotifen, the precursor of norketotifen, is known to be optically active, as pure enantiomers of ketotifen and their biological activities are described in Polivka I (pages 7-10, Examples 1, 3) and in Polivka II (page 2456-7). Accordingly, one of ordinary skill in the art would expect norketotifen to be optically active and the method for resolving the precursor ketotifen would be applicable for the separation of the S and R forms of norketotifen in view of their structural similarity. At the time of the invention, one of ordinary skill in the art would be motivated to resolve the optical isomers of the norketotifen of the patent and prepare the pharmaceutical composition comprising the optically isomer, such as the S-isomer of norketotifen to arrive at the instant invention.

Conclusion

11. Claim 6 is allowed. The instant method of making the R or S norketotifen is not anticipated or rendered obvious by the prior art of record.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625